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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,701	12/11/2006	Karin Ekberg	CBX0007-506-US	3695

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EXAMINER	
MACFARLANE, STACEY NEE	
ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
12/11/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/575,701	EKBERG ET AL.	
	Examiner	Art Unit	
	STACEY MACFARLANE	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3 and 10-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3 and 10-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/18/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims 3, 10 and 12-14 have been amended as requested in the amendment filed on September 18, 2009. Following the amendment, claims 3 and 10-15 are pending in the instant application, and are under examination in the instant office action.

2. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

3. Applicant's arguments filed on September 18, 2009 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 3, 10 and 12-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Johansson et al., Diabetologia, 35:121-128 (1992).

6. Claims 3, 10 and 12-15 are drawn to a method of treating diabetes and/or diabetes-related microvascular complications comprising administering C-peptide or a pharmaceutical composition comprising C-peptide to a patient once daily, wherein said once daily administration does not include continuous administration of the presence of rate-controlling agents (claim 3); wherein the C-peptide is human (claim 10); the patient

is human (claim 12); the composition contains 100 to 1800 nmol of c-peptide (claim 13); and the complications are nephropathy, retinopathy or neuropathy (claim 14).

7. With respect to the "once daily dose" of the claims, the specification states:

[0025] Reference to a `once daily dose` or `once daily administration` means, of course, not only that the medicament itself is only given once per day but that the patient receives no other C-peptide treatment. Such instructions may be made clear by the prescribing physician and/or in literature accompanying the packaged medication. The medicament may be adapted for once daily administration. This does not imply the presence of substances which act as release rate controlling agents, indeed the most preferred formulation of the invention is an uncompromised aqueous solution. However, the fact that a single, rather than multiple, dose is given may be reflected in the amount of active agent administered in the single dose, which may be more than would typically be administered in a dose prepared for thrice daily administration for example. Thus, different amounts may be given in a single dose, which may be greater than the amounts which would be administered in a dose intended for administration more than once. Thus, a single dose may have a higher concentration of active agent or the dose may be administered in a greater amount, e.g. a greater volume. Specific doses are described below. A once daily dose does not cover a continuous administration and is distinct therefrom. A once daily dose hence is directed to only one administration per day of the C-peptide treatment whereas a continuous administration would be constantly administering C-peptide treatment, or administering it over a prolonged period of time.

There is no explicit definition provided for the "rate-controlling agents" of the claims, nor is there explicit guidance as to what constitutes "continuous administration" or "prolonged period of time". Absent specific guidance within the disclosure, the claim is interpreted as encompassing a once daily administration, by any mode other than osmotic pump and excluding infusions that go beyond the bounds of 24 hours ("daily" of the claims).

8. The Johansson et al. reference discloses method of treating renal function ("nephropathy") complications in type 1 diabetics comprising a single administration of C-peptide. Specifically, 11 Type 1 diabetic human patients were given a 2 hour

intravenous administration of human recombinant C-peptide (paragraph bridging pages 122-123). The reference teaches the 120 minute administration comprises a total of 2.538 nmol/kg of C-peptide, which for the average person (150 pounds=68 kilograms), would be a total pharmaceutical composition of ~172 nmol C-peptide and within the range required by claim 13. Thus, the method of the invention fails to distinguish over that within the prior art disclosure.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. As currently amended, Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Johansson et al. (1992) as applied to claims 3, 10 and 12-15 above, and further in view of Wahren et al., (1998) cited in the previous Office action.

The Johansson et al. reference discloses method of treating renal nephropathy complications in type 1 diabetic human patients comprising a single administration of human recombinant C-peptide within the range of 100 to 1800 mnol. The Johansson et al. reference does not teach administration wherein the C-peptide is a fragment EGSLQ (SEQ ID NO: 2). The Wahren et al. reference, however, teaches that the fragment consisting of SEQ ID NO: 2 (which is identical to SEQ ID NO: 3 or "Peptide E" of Wahren reference) has the same stimulatory activity and molecular effect as full-length C-peptide (Example 1).

In *KSR International Co. v. Teleflex, Inc.*, the Supreme Court has stated that combining prior art elements according to known method to yield predictable results is *prima facie* obvious if the following rationale can be applied:

> (1) the prior art includes each element claimed though not necessarily in the same reference.
>
> (2) it was within the technical grasp of one of ordinary skill in the art to combine the elements as claimed by known methods, and that in combination, each element merely would have performed the same function as it did separately.
>
> (3) one of ordinary skill in the art would have recognized that the results of such combination were predictable.

(KSR International Co. v. Teleflex, Inc. 127 S. Ct. 1727, 82 USPQ2d 1385, Supreme Court, April 30, 2007).

One of ordinary skill in the art would recognize the use of the EGSLQ pentapeptide fragment, equivalent to claimed SEQ ID NO: 2, taught by Wahren et al. in the method of Johansson et al. A skilled artisan would be motivated to combine the prior art elements because this specific fragment maintains the stimulatory activity and thus would result in the predictable effect of treating diabetic renal nephropathy. Based upon the guidance and direction within the prior art, such combination would have been

well within the technical grasp of a skilled artisan. Since each of the elements in combination are merely performing the same function as they did separately, then one of ordinary skill in the art would have been able to predictably combine the elements with a reasonable expectation of success. Therefore, the invention as a whole is *prima facie obvious*, if not actually anticipated by the reference.

Conclusion

12. No claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is (571)270-3057. The examiner can normally be reached on M-W and F 5:30 to 2, TELEWORK-Thursdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane
Examiner
Art Unit 1649

/John D. Ulm/
Primary Examiner, Art Unit 1649